OPEN ACCESS Freely available online

Journal of Cancer Science and Research

Commentary

Hybrid Nanomedicines Combining Chemotherapy and Autophagy Modulation

Elenam Rossy*

Department of Molecular Pharmacology, University of Milan, Milan, Italy

DESCRIPTION

Cancer treatment continues to face substantial challenges due to drug resistance, tumour heterogeneity, and systemic toxicity associated with conventional chemotherapy. Despite advancements in chemotherapeutic agents, the effectiveness of these treatments is often limited by the ability of tumour cells to adapt and survive under stress conditions. One mechanism by which cancer cells evade chemotherapeutic killing is autophagy, a cellular process that degrades and recycles damaged organelles and proteins, providing energy and maintaining cellular homeostasis. While autophagy can promote cell death under certain conditions, many tumours exploit this process to survive therapeutic stress. Recent developments in nanomedicine have enabled the design of hybrid systems that combine chemotherapeutic agents with molecules capable of modulating autophagy, offering a promising strategy to overcome resistance and improve treatment outcomes.

Hybrid nanomedicines are engineered nanoparticles designed to deliver multiple therapeutic agents simultaneously. These systems can carry chemotherapeutic drugs alongside autophagy modulators, allowing for coordinated and controlled release directly to tumour cells. By encapsulating both agents within a single nanosystem, hybrid nanomedicines enhance drug accumulation at the tumour site, reduce off target toxicity, and allow precise temporal control over drug release. The use of nanocarriers such as liposomes, polymeric nanoparticles, and inorganic nanoparticles provides structural stability, surface functionalization for tumour targeting, and stimuli responsive release triggered by factors such as pH, temperature, or enzymatic activity.

Chemotherapy remains a cornerstone of cancer treatment, functioning primarily by inducing DNA damage, disrupting cell division, and promoting apoptosis in rapidly dividing cells. However, the cytotoxic stress generated by chemotherapeutic agents often activates protective autophagy in tumour cells, which can counteract therapy and lead to drug resistance. By incorporating autophagy modulators into nanomedicine systems, it is possible to either inhibit or enhance autophagy depending on the therapeutic goal. In many cases, autophagy inhibitors, such as chloroquine derivatives, are employed to block the protective mechanism, rendering tumour cells more susceptible to chemotherapeutic induced apoptosis. Conversely, in certain contexts, autophagy inducers may be used to push cells into autophagic cell death, creating an alternative cytotoxic pathway.

Targeted delivery and tumour specific accumulation are crucial for the success of hybrid nanomedicines. Surface modification of nanoparticles with ligands recognizing tumour associated receptors allows selective uptake by cancer cells while sparing healthy tissue. For example, folate, transferrin, or peptide based targeting moieties can enhance the internalization of nanoparticles in specific tumour subtypes. In addition, stimuli responsive designs enable the controlled release of chemotherapeutic drugs and autophagy modulators within the tumour microenvironment, minimizing systemic exposure and toxicity. These strategies collectively improve the therapeutic index and reduce adverse effects commonly associated with conventional chemotherapy.

Another advantage of hybrid nanomedicines is the ability to overcome multidrug resistance, a common obstacle in cancer therapy. Tumour cells often express efflux pumps that expel chemotherapeutic drugs, reducing intracellular drug concentrations and diminishing efficacy. Encapsulation of chemotherapeutic agents within nanoparticles protects them from efflux and degradation, enhancing intracellular accumulation. Moreover, autophagy modulation can impair survival mechanisms that allow resistant cells to persist under therapeutic stress, sensitizing them to chemotherapy and promoting cell death.

Translating hybrid nanomedicines from preclinical models to clinical application requires careful consideration of safety, biocompatibility, and pharmacokinetics. Nanoparticles must be biodegradable, non immunogenic, and capable of being cleared from the body without causing long term accumulation or organ toxicity. Comprehensive characterization of nanoparticle size, surface charge, and stability is essential for reproducibility and regulatory approval. In addition, optimization of dosing schedules and combination ratios of chemotherapeutic drugs and autophagy modulators is critical to maximize synergistic effects while minimizing adverse reactions.

Correspondence to: Elenam Rossy, Department of Molecular Pharmacology, University of Milan, Milan, Italy, E-mail: elena26rossi@unimi.it

Received: 02-May-2025, Manuscript No. JCSR-25-39004; **Editor assigned:** 16-May-2025, PreQC No. JCSR-25-39004 (PQ); **Reviewed:** 23-May-2025, QC No. JCSR-25-39004; **Revised:** 30-May-2025, Manuscript No. JCSR-25-39004 (R); **Published:** 06-Jun-2025, DOI: 10.35248/2576-1447.25.10.627

Citation: Rossy E (2025 Hybrid Nanomedicines Combining Chemotherapy and Autophagy Modulation. J Can Sci Res. 10:627.

Clinical studies investigating hybrid nanomedicines are still in early stages, but initial findings are encouraging. For instance, polymeric nanoparticles co delivering paclitaxel and autophagy inhibitors have shown improved response rates in solid tumour patients with manageable side effect profiles. These results support further development and suggest that personalized approaches, guided by tumour autophagy status and genetic characteristics, may enhance the effectiveness of hybrid nanomedicines. Integration with other therapeutic modalities, such as immunotherapy or radiation therapy, may further improve outcomes by combining multiple mechanisms of tumour cell killing.

Mechanistic insights into hybrid nanomedicines reveal that the combination of chemotherapy and autophagy modulation affects several interconnected pathways within cancer cells. Disruption of autophagic flux increases cellular stress and accumulation of reactive oxygen species, leading to mitochondrial dysfunction and activation of intrinsic apoptotic pathways. Concurrently, chemotherapeutic agents induce DNA damage and mitotic arrest, further amplifying cell death signals. The interplay between these pathways enhances the overall cytotoxic effect and reduces the likelihood of tumour cells surviving therapy. Furthermore, modulation of autophagy can influence the tumour immune microenvironment, potentially enhancing immune recognition and clearance of cancer cells.

CONCLUSION

Hybrid nanomedicines combining chemotherapy and autophagy modulation represent a promising strategy to overcome resistance, enhance tumour cell killing, and improve therapeutic outcomes in cancer treatment. By enabling targeted, controlled, and synergistic delivery of multiple agents, these nanosystems address key limitations of conventional chemotherapy. Preclinical studies demonstrate enhanced tumour regression, increased apoptosis, and improved survival with combination therapy. Careful optimization of nanoparticle design, drug ratios, and delivery strategies is essential for clinical translation. Ongoing research and clinical trials will continue to elucidate the full potential of hybrid nanomedicines and may establish them as a next generation approach in personalized cancer therapy, offering hope for patients with resistant and aggressive tumours.